Summary

1) Pilocarpine induced TLE rats were used as a model to study the alterations of serotoninergic, ionotropic and metabotropic receptors and their functional regulation by Bacopa monnieri. It was used to study the serotonin, 5-HT$_{2C}$ and NMDA receptor alterations in the epileptic rats, Bacopa monnieri and carbamazepine treatment to epileptic rats.

2) The body weight, feed and water intake was carried out to analyze the changes in body weight, feed and water consumption due to seizures in epileptic rats compared to control and effect of Bacopa monnieri and carbamazepine treatment to epileptic rats. Epilepsy caused a reduction in the body weight, food and water consumption. Bacopa monnieri and carbamazepine treatment to epileptic rats reversed the changes to near control.

3) Blood glucose level in the serum was measured to analyze the circulating glucose level changes due to seizures in epileptic rats compared to control and the effect of Bacopa monnieri and carbamazepine treatment to epileptic rats. Epilepsy did not cause any significant change in the circulating blood glucose level of epileptic rats. There was no significant change in the circulating blood glucose of epileptic rats after treatment with Bacopa monnieri and carbamazepine.

4) The 5-HT and 5-HIAA contents were measured to identify its alteration in the cerebral cortex, hippocampus, cerebellum and brainstem in epileptic rats compared to control and effect of Bacopa monnieri and carbamazepine treatment to epileptic rats using High Performance Liquid Chromatography.
a. Significant decrease in 5-HT content in the cerebral cortex, hippocampus, cerebellum and brainstem was observed in epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the 5-HT content to control level.

b. 5-HIAA content significantly increased the cerebral cortex, hippocampus, cerebellum and brainstem of epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* treatment to epileptic rats reversed the changes to near control level.

c. 5-HT/5-HIAA ratio decreased significantly in the cerebral cortex, hippocampus, cerebellum and brainstem of epileptic compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* treatment to epileptic rats reversed the changes to control in cerebral cortex and cerebellum.

5) 5-HT$_{2C}$ receptor functional status was analysed by Scatchard analysis using [³H]mesulergine in cerebral cortex, hippocampus, brainstem and cerebellum. Receptor gene expression was confirmed by Real-Time PCR. The 5-HT$_{2C}$ receptors in cerebral cortex and hippocampus showed a significant increase in epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the changes to control.

6) NMDA receptor functional status was analysed by Scatchard analysis using [³H]MK-801 in cerebral cortex, hippocampus, cerebellum and brainstem. Receptor gene expression was confirmed by Real-Time PCR. The NMDA receptors were decreased in cerebral cortex and hippocampus while it showed a significant increase in cerebellum and brainstem of epileptic rats compared to
control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the changes to control. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the receptor status towards control values.

7) The NMDA2b receptor genes showed down regulation in cerebral cortex, hippocampus while it was up regulated in cerebellum and brainstem of epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. This was reversed to control values with *Bacopa monnieri* and carbamazepine treatment which confirmed the receptor data.

8) The mGLU5 gene was up regulated in cerebral cortex, hippocampus, cerebellum and brainstem of epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the changes to near control.

9) The GLAST gene expression was found to be increased in cerebral cortex, hippocampus and brainstem while it was found to be decreased in cerebellum of epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. This was reversed to control values with *Bacopa monnieri* and carbamazepine treatment.

10) The IP3 levels increased significantly in cerebral cortex, hippocampus and brainstem while it decreased significantly in cerebellum of epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. This was reversed to control values with *Bacopa monnieri* and carbamazepine treatment.
11) The cGMP levels increased significantly in hippocampus, cerebellum and brainstem while it showed a significant decrease in cerebral cortex of control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the changes to control values.

12) The cAMP levels increased significantly in the cerebral cortex and hippocampus while decreased significantly in cerebellum and brainstem of control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the changes to control values.

13) Behavioural studies of the experimental groups of rats were carried out using rotarod test, elevated plus maze test, forced swim test and social interaction test were conducted to assess the changes in the motor and anxiodepressive states.

- The Rotarod experiment demonstrated the impairment in the motor function and coordination in the epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. This was reversed to control values with *Bacopa monnieri* and carbamazepine treatment to epileptic rats.

- Elevated plus maze and social interaction test implicate a role for 5-HT$_{2c}$ receptors in the manifestation of anxiety in the epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* treatment to epileptic rats was found to have anxiolytic properties.

- Forced swim test confirmed the depressive traits in the epileptic rats compared to control rats and *Bacopa monnieri* treated control rats. *Bacopa monnieri* and carbamazepine treatment to epileptic rats reversed the alterations to near control.
Summary

14) The 5-HT\textsubscript{2C}, NMDA2b and mGlu5 receptor changes in the cerebral cortex and cerebellum were confirmed by confocal studies using receptor specific antibodies in the brain slices.

Our results demonstrate changes in the brain 5-HT\textsubscript{2C} receptors play a significant role in the motor dysfunction, seizure activity, anxiety and depression during epilepsy. Alterations in the NMDA receptor function lead to seizures, memory and cognitive deficits in brain. *Bacopa monnieri* treatment to epileptic rats significantly reversed these alterations. *Bacopa monnieri* treatment to epileptic rats was effective in neurotransmitter receptor functional regulation in controlling seizures, improving motor function and enhancing the cognitive functions in epileptic rats mediated through 5-HT\textsubscript{2C} and NMDA receptors. Thus it is evident that *Bacopa monnieri* treatment to epileptic rats renders protection against seizure related excitotoxicity, associated with motor and cognitive deficits. These findings will have clinical significance in the management of epilepsy.